WE CLAIM:

1. A non-viral gene modification method for incorporating a single stranded end-capped oligonucleotide with improved incorpoation efficiency into a target population of cells comprising:
    a. preparing a formulation comprising a single stranded end-capped oligonucleotide having a nucleic acid sequence of interest corresponding to a sequence of interest to be modified in a target population of cells, wherein said sequence of interest to be modified comprises 1 to 50 bases;
    b. immobilizing the target population of cells onto a substrate to provide an adherent target population of cells;
    c. incorporating the single stranded end-capped oligonucleotide into the target population of cells to provide genetically modified cells; and
    d. detaching said population of genetically modified cells from said substrate,

    wherein greater than about 0.0001% of the target population of cells does not include the unmodified nucleic acid sequence.

2. The method of claim 1 wherein the nucleic acid sequence of interest comprises a wild-type nucleic acid sequence corresponding to an identified mutated nucleotide base or nucleotide bases of the target population of cells.

3. The method of claim 1 wherein the nucleic acid sequence of interest encodes β-globin.

4. The method of claim 1 wherein said single stranded end-capped oligonucleotide is defined at SEQ ID: No. 1.

5. The method of claim 4 wherein the end caps of the small single stranded oligonucleotides include, but are not limited to, phosphorothioate linkages between nucleotides, a backbone of methylphosphonate, phosphoramididate,

morpholino peptide linkages, or nucleotides containing different 2'-halo, 2'-alkyl, or 2'-alkoxylalklyl sugars.

6. The method of claim 4 wherein the single-stranded end-capped oligonucleotide molecule has a sequence length of between 10 to 200 nucleotide bases.

7. The method of claim 1 wherein said formulation further comprises macromolecules, foreign materials, or exogenous molecules that enhance the efficiency and/or efficacy of gene modification.

8. The method of claim 7 wherein said macromolecule is a protein, a peptide fragment of said protein, a recombinant portion of said protein, or a combination thereof.

9. A cell population comprising an enriched population of genetically modified cells having a targeted gene modification artificially created using a single stranded end-capped oligonucleotide, wherein said targeted gene modification comprises a sequence of 10 to 200 nucleotides.

10. The cell population of claim 9 wherein said genetically modified cells include primary cell types, a transformed cell line, a non-transformed cell line, or a combination thereof.

11. The cell culture of claim 10 wherein said genetically modified cells normally exist in a suspended/non-adherent state.

12. The cell culture of claim 10 wherein said genetically modified cells are mammalian somatic cells.

13. The cell culture of claim 10 wherein said genetically modified cells are plant cells.

14. A transgenic animal having a site-specific genetic modification, wherein said genetic modification is provided using a single stranded end-capped oligonucleotide molecule, wherein said molecule comprises a sequence of between 10 and 200 nucleotide bases.

15. The transgenic animal of claim 14, wherein the site-specific genetic modification comprises a modification in mouse embryonic stem (ES) cells or similar cells genetically modified.

16. The non-viral gene modification method of claim 1 wherein said target cell population are somatic human hematopoietic stem/progenitor cells.

17. The non-viral gene modification method of claim 1 wherein said target population of cells are somatic human stem cells further defined as precursors of liver, pancreatic, mesenchymal, endothelial, muscle, or neuronal cells.

18. The non-viral gene modification method of claim 1 wherein the formulation is incorporated into the adherent target population of cells by needle-mediated microinjection.

19. The non-viral gene modification method of claim 1 wherein the formulation comprising the single stranded end-capped oligonucleotide is incorporated into the adherent target population of cells by electroporation, dendrimers, cationic liposome-mediated transfection, particle bombardment, iontophoresis, peptide-mediated nucleic acid delivery, red blood cell-mediated transfection, hypotonic swelling, micropricking, laser mediated introduction including the laser scissor method, and addition of the nucleic acid molecules directly to the medium surrounding the cells.

20. The non-viral gene modification method of claim 1 wherein the formulation incorporated into the cells comprises accessory oligonucleotides that enhance the efficiency and/or efficacy of gene modification.

21. The non-viral gene modification method of claim 1 further defined as a gene repair method wherein the target population of cells comprises mutant cells having an identifiable genetic mutation of from 1 to 200 bases relative to a wild-type sequence.

22. The non-viral gene modification method of claim 21 wherein the mutant cells include a mutated nucleic acid sequence with 1 to 50 mutant bases relative to a wild-type sequence.

23. The non-viral gene modification method of claim 22 wherein the mutated nucleic acid sequence comprises 1 to 20 mutant bases relative to the wild-type sequence.

24. The non-viral gene modification method of claim 23 wherein the mutated nucleic acid sequence comprises 1 to 10 mutant bases relative to the wild-type sequence.

25. The non-viral gene modification method of claim 24 wherein the mutated nucleic acid sequence comprises 1 to 5 mutant bases relative to the wild-type sequence.

26. The non-viral gene modification method of claim 25 wherein the mutated nucleic acid sequence comprises 2 mutant bases relative to the wild-type sequence.

27. The non-viral gene modification method of claim 26 wherein the mutated nucleic acid sequence is a single point mutation relative to the wild-type sequence.

28. The non-viral gene modification method of claim 21 wherein the mutated nucleic acid sequence of said target population of cells comprises the sequence at Gen. Bank Accession No. P19885.

29. A non-viral mediated method for the incorporation of a single stranded end-capped oligonucleotide with improved incorporation efficiency into a target population of cells comprising:

a. preparing a formulation comprising a single stranded end-capped oligonucleotide having a nucleic acid sequence of interest corresponding to a mutated sequence counterpart of a wild-type target gene of interest , wherein said mutated sequence comprises 1 to 50 mutant bases relative to a wild-type sequence;

b. immobilizing the population of wild-type cells to a substrate to provide adherent target cells;

c. incorporating the single stranded end-capped oligonucleotide into the adherent wild-type target cells to provide a population of genetically modified target cells comprising a mutant nucleic acid sequence; and

d. detaching said population of genetically modified cells from said substrate, wherein modified cell population comprises mutant cells that do not include the wild-type nucleic acid sequence corresponding to the mutated nucleic acid sequence, or mutant cells containing one allele with the mutant sequence and one allel with the wild type sequence.

30. The non-viral mediated method of claim 29 wherein the mutated nucleic acid sequence comprises 1 to 100 mutant nucleotides relative to the wild-type sequence.

31. The non-viral mediated method of claim 29 wherein the mutated nucleic acid sequence comprises 1 to 50 mutant nucleotides relative to the wild-type nucleic acid sequence.

32. The non-viral mediated method of claim 29 wherein the mutated nucleic acid sequence comprises 1 to 20 mutant nucleotides relative to the wild-type sequence.

33. The non-viral mediated method of claim 29 wherein the mutated nucleic acid sequence comprises 1 to 10 mutant nucleotides relative to the wild-type sequence.

34. The non-viral mediated method of claim 29 wherein the mutated nucleic acid sequence comprises 1 to 5 mutant nucleotides relative to the wild-type sequence.

35. The non-viral mediated method of claim 29 wherein the mutated nucleic acid sequence comprises 2 mutant nucleotides relative to the wild-type sequence.

36. The non-viral mediated method of claim 29 wherein the mutated nucleic acid sequence comprises 1 mutant nucleotide relative to the wild-type sequence.

37. The non-viral mediated method of claim 29 wherein the target population of cells comprises primary cells types, transformed, or non-transformed mammalian somatic cells.

38. The non-viral mediated method of claim 29 wherein said modified cells exist in a suspended/non-adherent state.

39. The non-viral mediated method of claim 37 wherein the target population of cells comprise endothelial cells.

40. The non-viral mediated method of claim 37 wherein the target population of cells comprise somatic stem cells including, but not limited to, hepatic, neuronal, endothelial, or mesenchymal stem cells.

41. The non-viral mediated method of claim 37 wherein the target population of cells comprise murine (mouse) embryonic stem cells.

42. The non-viral mediated method of claim 29 wherein the target population of cells comprise plant cells.

43. The method of claim 42 wherein the substrate for attachment of the target population of plant cells includes, but is not limited to, plant lectin binding carbohydrates, agarose, agar, their derivatives, or combinations thereof.